Synopsis

Regarding the clinical trial

The effects of intravenous iron on mobility in elderly patients following hip fracture surgery: a multicentre, parallel group, randomised controlled trial

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Title: The effects of intravenous iron on mobility in elderly patients following hip fracture surgery: multicentre, parallel group, randomised controlled trial

Short Title: The IronHip Trial

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Background: Mobility impairment is a significant issue in elderly patients recovering from hip fracture surgery. Anaemia is common in this population and contribute to reduced physical function and delayed recovery. This study aims to evaluate the effectiveness of intravenous iron supplementation in improving mobility outcomes post-surgery.

Primary objective: To assess the impact of Ferric derisomaltose (FDI), relative to placebo, on functional mobility measured with New Mobility Score (NMS) in elderly patients following hip fracture surgery after 6 weeks.

Secondary objectives: To evaluate the effects of FDI, relative to placebo, on haemoglobin correction, transfusion use, fatigue, quality of life, fear of falls, 30 second Sit-to-Stand-Test activities of daily living, pain, health resources, SAE, and mortality.

Trial configuration: This is a multicentre, parallel group, randomised, controlled trial designed to compare the effects of FDI versus standard care in elderly patient's post-hip fracture surgery. Outcome measures will be collected at baseline (t=0), 4, 6, 12 weeks and 90 days from baseline.

Setting: The trial will be conducted across three hospital departments in orthopaedic surgery and traumatology; Bispebjerg and Frederiksberg University Hospital, Odense and Svendborg University Hospital and Herlev and Gentofte University Hospital

Target population: Elderly patients, aged 65 and above, undergoing hip fracture surgery

Sample size estimate: We calculated that 172 elderly HF patients are needed in the intention-to-treat population to detect a 1 NMS point improvement with 90% power at a 5% significance level,

assuming a 2-point SD. To account for attrition and missing data, we plan to enrol at 210 patients in total (70 per centre; corresponding to 22% extra compared to the formal power requirement). The target difference aligns with a Minimal Important Difference (MID) of 1 NMS unit, based on previous studies.

Number of participants: 210

Eligibility criteria:

Inclusion

- 65 years of age or older
- Acute proximal femur fracture surgery
- A haemoglobin measurement ≤6.5 mmol/L (10.5 g/dL) on day 1 to 5 postoperatively
- Independent pre-fracture indoor walking ability; Indoor New Mobility Score ≥ 2
- Ability to speak and understand Danish
- Able to provide informed consent on their own behalf

Exclusion

- No known allergy to intravenous iron
- Residing permanently at a nursing home
- Haematological conditions with a risk of iron overload e.g. haemochromatosis, hemosiderosis, or where alternative treatments are necessary e.g. haematological malignancies
- Other contraindication to iron treatment, e.g. severe liver cirrhosis and hepatitis
- Severe uncontrolled infection as assessed by the responsible clinician (e.g. bacteraemia or sepsis)
- Plasma sodium levels below 125 or above 150 mmol/L on the day of inclusion
- Renal replacement therapy
- Severe dementia assessed by physician
- Recent intravenous iron injection, 4 weeks prior to surgery
- Patient declared terminal ill
- Pathologic Fracture

Description of interventions: Usual care: All recruitment departments will provide care aligned to national standards and guidelines. Usual care plus a single intravenous FDI (20 mg/kg body weight as a single dose on day 1-5 post surgery. Placebo: isotonic saline 100 ml plus usual care.

Choice of investigational medicine: FDI is chosen between different iv. Iron supplements because it has a well characterised safety profile, with low risk of hypophosphatemia and can be given in a high single dose.

Duration of trial: Participants will be followed for a period of 90 days with a phone call after 4 weeks, and an in-person visit at 6 and 12 weeks, to assess primary and secondary outcomes.

Randomisation and blinding: Participants will be randomly allocated to the intervention or control group in a 1:1 ratio, stratified by centre and fracture type, using a computer-generated randomization schedule. Blinding will be maintained for outcome assessors to minimize bias.

Primary outcome and endpoints: Patients will report their baseline NMS as pre-fracture at inclusion. NMS will be reassessed by phone at week 4, and in-person at weeks 6 and 12. The primary endpoint is NMS at 6 weeks, derived from the difference between least squares means, analysed using repeated-measures mixed linear models (with 4 time points).

Secondary outcomes: Haemoglobin**,** red blood cell transfusion**,** fatigue**,** quality of life**,** fear of falls**,** 30 second sit-to-stand-test, activity of daily living**,** pain**,** Days alive and at home up to 30, serious adverse events and mortality

Statistical methods: The main analysis will be based on the Intention to Treat (ITT) population, including all randomized individuals with a baseline measure. Participants will be analysed in their assigned groups regardless of treatment adherence. Missing data will be handled using repeated-measures linear mixed models, valid under the ‘Missing at Random’ (MAR) assumption. The primary endpoint is the difference in change in NMS from baseline to 6 weeks, using mixed linear models. All confidence intervals and P values will be two-sided, with a statistical significance level of 0.05.

Explorative outcomes: Cost-Effectiveness is analysed from a societal perspective. Data from patient will compare mean costs and incremental cost-effectiveness ratios between groups**. Physical Activity and strength**, measured with SENS motion monitors in 70 patients at Bispebjerg Hospital, tracking daily activity for 10 days at the 6-week follow-up, comparing average standing and walking time between groups. Strength measured with hand grip strength and knee extension. **Cognition** is Assessed with Orientation-Memory-Concentration test at baseline, and at weeks 6 and 12 post-intervention. **Biochemical response**: Ferritin, transferrin-saturation and hepcidin will be measured at baseline, and at week 6 and 12 to compare iron status between groups.

On behalf of the IronHip trial group

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